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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,822	11/01/2001	Alberto L. Mendoza	MSU 4.1-542	6022

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EXAMINER
MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
1645	7

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,822	MENDOZA, ALBERTO L.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 13-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-3 and 13-32* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 4sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group II, claims 4-12, in Paper No. 6 is acknowledged. The traversal is on the ground(s) that Group I (claims 1-3) and Group II (claims 4-12) should be combined since no reason is provided for separating these claims. Applicant also asserts that the Group I claims are generic to Group II claims and thus are not distinct inventions. This is not found persuasive because as previously stated in the Restriction Requirement the methods of Group I and II have different steps and parameters; Group II method claims have many additional preparation steps with regard to preparing the vaccine to be injected. Group I does not define or set forth steps with regard to how the vaccine is prepared, therefore the inventions are distinct.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-3 and 13-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention(s), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

3. The disclosure is objected to because of the following informalities: Table 1, the symbols in the "Outcome" column are not defined.

Appropriate correction is required.

4. The use of trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-12 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. The inclusion of 28, 30 and 32 kDa antigens from the intracellular cytoplasm in the vaccine appears to be critical or essential to the practice of the invention, but not included in the claim(s). See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The claims are directed to a method for treatment of pythiosis or prophylaxis against pythiosis in a mammal comprising providing a vaccine (intracellular cytoplasmic antigens and extracellular cytoplasmic antigens of *Pythium insidiosum*) and vaccinating the mammal with the vaccine. The claims also recite the method of preparation of the vaccine.

The specification discloses Example 1, the preparation of the PIV (*Pythium insidiosum* vaccine). The specification indicates that in come cases the 32, 30, and 28 kDa immunodominant antigens were purified by preparative SDS-PAGE and that the antigens were cut from the gels and purified. The 32, 30 and 28 kDa antigens were mixed to make a mixture which a portion of which was added to the

Mendoza vaccine to produce a modified Mendoza vaccine with a final protein concentration of about 2.0 micrograms/ml (see pages 21-22). Example 2 discloses a PIV evaluation in horses with pythiosis and that the present PIV is superior to the prior PIV of Mendoza. The specification states that the "results suggests that 1) the presence of the cytoplasmic antigens, which included the 32 kDa, 30 kDa, and 28 kDa immunodominant antigens, directly enhanced the efficacy of the Mendoza vaccine which always failed in chronic cases (>60 days)." (p. 23, lines 19-23) The results also suggest that the cytoplasmic antigens directly affect the immuno-therapeutic properties of the Mendoza vaccine and that the cytoplasmic antigens play a role in the immunology of *Pythium insidiosum* infection (p. 23, lines 25-28). Example 3 describes the production of mAb to the 32, 30 and 28 kDa antigens of intracellular cytoplasm of cells from *Pythium insidiosum*. Example 4 describes the cDNA preparation of 32, 30 and 28 kDa antigens of intracellular cytoplasm of cells from *Pythium insidiosum*. Example 5 discloses the successful treatment of a Thai boy using the PIV as prepared in Example 1. Example 6 describes testing of PIV on horses, dogs and a cat with pythiosis. The specification indicates that the PIV comprised the extracellular antigens and intracellular cytoplasmic antigens, which included the 28, 30 and 32 kDa antigens. Two injections were administered, one at day 0 and another at day 15. Additional injections were given to animals that did not show improvement with the first two vaccinations. 12 of 19 horses were considered cured, 5 of 19 horses were not cured while the other 2 horses either died or was sacrificed. Only one of 5 dogs was considered cured, the other 4 dogs were not cured, and the one cat was not cured. Example 7 illustrated the method for evaluation of PIV in a rabbit model.

It would appear that the PIV as taught in the specification is an admixture of intracellular cytoplasmic antigens, which include the 28, 30 and 32 kDa antigens and extracellular cytoplasmic antigens of cells from *Pythium insidiosum*. However, the present claims recite that the vaccine comprises intracellular cytoplasmic antigens and extracellular cytoplasmic antigens from cells of *Pythium insidiosum*). As previously noted from the specification, the 32, 30, and 28 kDa antigens of the intracellular cytoplasmic antigens appear to be very important in the efficacy and success of the PIV. The immunodominant proteins (32, 30 and 28 kDa) from the intracellular cytoplasm appear to be important and significant components for the vaccine composition, not intracellular cytoplasmic antigens, generically. The specification appears to enable a vaccine comprising three immunodominant proteins (32, 30 and 28 kDa) and extracellular proteins from cells of *Pythium insidiosum*, not the generically claimed admixture of intracellular cytoplasmic antigens and extracellular antigens from cells of *Pythium insidiosum*. It would appear that critical or essential elements of the vaccine are not recited in the claims but have been set forth in the specification. Therefore, based on the present specification, it is not clear if the claimed invention is enabled with regard to how to make and use the claimed invention.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 4-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza et al (1992, J. Clinical Microbiology, 30/11:2980-2983) taken with Mendoza et al (1992, Micropathologia, 119:89-95).

The claims are directed to a method for treatment of pythiosis or prophylaxis against pythiosis in a mammal comprising providing a vaccine (intracellular

cytoplasmic antigens and extracellular cytoplasmic antigens of *Pythium insidiosum*) and cytoplasmic antigens, which included the 28, 30 and 32 kDa antigens vaccinating the mammal with the vaccine. The claims also recite the method of preparation of the vaccine.

Mendoza et al (J. Clinical Microbiology) teaches vaccines prepared from various antigens (proteins) derived from *Pythium insidiosum* (ATCC 58643) and that the organism was grown in Sabouraud broth (materials and methods, p. 2980). The prior art also teaches the methods of filtration, solubilization, sonication and centrifugation (p. 2981, left hand column). The prior art teaches the inactivation of the proteins using thimerosal/merthiolate (p. 2981). The art teaches that "... the supernatant was collected and used to provide antigens." (p. 2981). The art further teaches filtration by PM-10 membranes, which removes less than 10,000 molecular weight components. The second supernatant obtained after sonication contained soluble antigens and/or intracellular proteins. Mendoza et al teaches the investigation of antigens from *P. insidiosum,* which may be important in the immune response of horses (i.e. mammals) to *P. insidiosum* infection (p. 2980, right hand column). The prior teaches the claimed invention except for the use of extracellular proteins.

However, Mendoza et al (Micropathologia) teaches the evaluation and production of two vaccines, cell-mass vaccine and soluble concentrated antigen (intracellular proteins), both of which have been derived from cells of *Pythium insidiosum* (ATCC 58643) and the organism was grown in Sabouraud broth (abstract; materials and methods). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the two supernatants (supernatants containing intracellular cytoplasmic and extracellular

proteins) of the two prior art references with a reasonable expectation of success of obtaining a vaccine for the treatment of infection caused by *Pythium insidiosum*. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the vaccines since both references teach the importance of preparing a vaccine for the treatment of infections caused by *Pythium insidiosum*; both the extracellular and intracellular cytoplasmic proteins have been found to be useful as vaccines to treat infection caused by *Pythium insidiosum*. Both vaccines of the prior art provide protection and cured the horses. The two vaccines of the prior art function in the same manner as the method of treating pythiosis or prophylaxis against pythiosis in a mammal comprising administering the same vaccine composition as claimed by Applicant. It would have been obvious to a person of ordinary skill in the art to combine both these vaccines into one vaccine for the purpose of providing better cure rates and protection to the animals. It is prima facie obvious to combine two compounds each of which is taught by the prior art references to be useful for the same purpose, the idea of combining them flows logically from their having been individually taught in the prior art. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

10. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
August 4, 2003